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# Assessment of "T2D Remission" Status of a Long-Term Type 2 Diabetes Patient Using the 2021 Consensus Report Sponsored by American Diabetes Association Based on GH-Method: Math-Physical Medicine (No. 505)

**Gerald C Hsu**

*EclaireMD Foundation, USA*

***Corresponding author**
Gerald C Hsu, EclaireMD Foundation, USA

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## Abstract

*The author has suffered from type 2 diabetes (T2D) for over 26 years and had complications related to his heart, kidney, eyes, foot, bladder, thyroid, etc. In 1995, he started taking Metformin, which led to two additional types of diabetes medications in high dosages. It took him three years to gradually decreased the dosages for each medication from 2013 to 2015, and ceased all of them on 12/8/2015. He started to implement a lifestyle management program step-by-step in mid-2015 at a slow and steady pace. His lifestyle program not only focuses on diet and exercise but also factors in sleep, stress, life habits, and environmental factors. This introduction is a brief overview of his long history of diabetes fighting. A detailed personal history of the author can be found in the methods section.*

*On 9/1/2021, he read a consensus report regarding the definition and interpretation of remission in T2D published on 8/30/2021. He wondered where was his standing according to the new guidelines described in this consensus report? Therefore, he must reorganize his collected personal big data (>2 million) according to the definition of "remission" which includes timespan requirements, HbA1C severity, fasting plasma glucose (FPG) level, estimated HbA1C (eA1C) values based on both mean finger glucoses and mean continuous glucose monitoring (CGM) glucoses. In addition, he sorted his collected mean carbohydrates & sugar intake amount per meal (positive stimulator for energy infusion) and mean post-meal walking steps per meal (negative stimulator for energy consumption) which are closely related to his glucoses.*

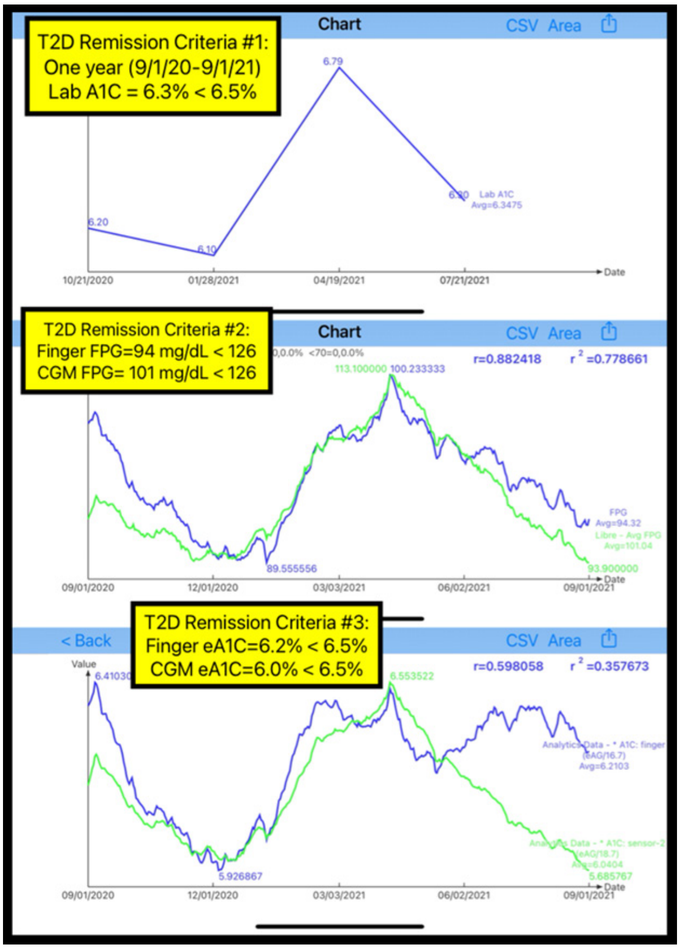
***In conclusion, according to the American Diabetes Association (ADA) 2021 consensus report, the author is in a "remission" state of T2D.*** *In summary, over the selected one-year period from 9/1/2020 to 9/1/2021, his average Lab-A1C is 6.3%, FPG values are 94 mg/dL (finger FPG) and 101 mg/dL (CGM FPG), and CGM eAG is 6.0%.*

*First, his selected timespan of past one year satisfies the timespan requirement from 2021 consensus report. This set of his glucose data is almost 5 years post-cessation of his medication intervention and initiation of his stringent lifestyle management program.*

*Second, all of his A1C values are less than 6.5% and his FPG levels are less than 126 mg/dL.*

*Finally, he has kept his regular routines of having quarterly medical examinations to watch out for various diabetes complications, including macro-vascular, micro- vascular, neural, and hormone systems.*

***He understands and agree with the consensus report that diabetes is non-curable and at most it is "controllable" or "partially reversible". Nevertheless, as a personal decision made in 2010, he has adopted a lifestyle improvement approach of dealing with the root causes of metabolic disorders, instead of suppressing the external symptoms of diseases through different medical treatments, including both medication and surgery.***




## Introduction

The author has suffered from type 2 diabetes (T2D) for over 26 years and had complications related to his heart, kidney, eyes, foot, bladder, thyroid, etc. In 1995, he started taking Metformin, which led to two additional types of diabetes medications in high dosages. It took him three years to gradually decreased the dosages for each medication from 2013 to 2015, and ceased all of them on 12/8/2015. He started to implement a lifestyle management program step-by-step in mid-2015 at a slow and steady pace. His lifestyle program not only focuses on diet and exercise but also factors in sleep, stress, life habits, and environmental factors. This introduction is a brief overview of his long history of diabetes fighting. A detailed personal history of the author can be found in the methods section.

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## Methods

### MPM Background

To learn more about his developed GH-Method: math-physical medicine (MPM) methodology, readers can read the following three papers selected from his ~500 published medical papers.

The first paper, No. 386 describes his MPM methodology in a general conceptual format. The second paper, No. 387 outlines the history of his personalized diabetes research, various application tools, and the differences between biochemical medicine (BCM) approach versus the MPM approach. The third paper, No. 397 depicts a general flow diagram containing ~10 key MPM research methods and different tools.

### The Author'S Case of Diabetes and Complications

The author has been a severe T2D patient since 1996. He weighed 220 lb. (100 kg, BMI 32.5) at that time. By 2010, he still weighed 198 lb. (BMI 29.2) with an average daily glucose of 250 mg/dL (HbA1C of 10%). During that year, his triglycerides reached to 1161 (diabetic retinopathy or DR) and albumin-creatinine ratio (ACR) at 116 (chronic kidney disease or CKD). He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him regarding his needs of kidney dialysis treatment and future high risk of dying from severe diabetic complications. Other than cerebrovascular disease (stroke), he has suffered most known diabetic complications, including both macro-vascular and micro-vascular complications.

In 2010, he decided to launch his self-study on endocrinology, diabetes, and food nutrition in order to save his own life. During 2015 and 2016, he developed four prediction models related to diabetes conditions: weight, PPG, fasting plasma glucose (FPG), and A1C. As a result, from using his developed mathematical metabolism index (MI) model in 2014 and the four prediction tools, by end of 2016, his weight was reduced from 220 lbs. (100 kg, BMI 32.5) to 176 lbs. (89 kg, BMI 26.0), waistline from 44 inches (112 cm, nonalcoholic fatty liver disease /NAFLD) to 33 inches (84 cm), average finger glucose reading from 250 mg/dL to 120 mg/dL, and lab-tested A1C from 10% to ~6.5%. One of his major accomplishments is that he no longer takes any diabetes medications since 12/8/2015.

In 2017, he has achieved excellent results on all fronts, especially his glucose control. However, during the pre-COVID period of 2018 and 2019, he traveled to approximately 50+ international cities to attend 65+ medical conferences and made ~120 oral presentations. This hectic schedule inflicted damage to his diabetes control, through dinning out frequently, post-meal exercise disruption, jet lag, and along with the overall metabolism impact due to his irregular life patterns through a busy travel schedule; therefore, his glucose control and overall metabolism state were somewhat affected during this two-year heavier traveling period.

During 2020 with a COVID-19 quarantined lifestyle, not only has he published ~400 medical papers in 100+ journals, but he has also reached his best health conditions for the past 26 years. By the beginning of 2021, his weight was further reduced to 165 lbs. (BMI 24.4) along with a 6.1% A1C value (daily average glucose at 105 mg/dL), without having any medication interventions or insulin injections. These good results are due to his non-traveling, low-stress, and regular daily life routines. Due to his knowledge of chronic diseases, practical lifestyle management experiences, and developed various high-tech tools contribute to his excellent health status since 1/19/2020, which is the start date of being self-quarantined.

On 5/5/2018, he applied a CGM sensor device on his upper arm and checks glucose measurements every 5 minutes for a total of ~288 times each day. He has maintained the same measurement pattern to present day. In his research work, he uses the CGM sensor glucose at time-interval of 15 minutes (96 data per day). By the way, the difference of average sensor glucoses between 5-minute intervals and 15-minute intervals is only 0.4% (average glucose of 114.81 mg/dL for 5-minutes and average glucose of 114.35 mg/dL for 15-minutes with a correlation of 93% between these two sensor glucose curves) during the period from 2/19/20- to 8/13/21.

Therefore, over the past 11 years, he could study and analyze the collected 2+ million data regarding his health status, medical conditions, and lifestyle details. He applies his knowledge, models, and tools from mathematics, physics, engineering, and computer science to conduct his medical research work. His medical research work is based on the aims of achieving both "high precision" with "quantitative proof" in the medical findings.

The following timetable provides a rough sketch of the emphasis of his medical research during each stage:

- 2000-2013: Self-study diabetes and food nutrition, developing a data collection and analysis software.
- 2014: Develop a mathematical model of metabolism, using engineering modeling and advanced mathematics.
- 2015: Weight & FPG prediction models, using neuroscience.
- 2016: PPG & HbA1C prediction models, using optical physics, artificial intelligence (AI), and neuroscience.
- 2017: Complications due to macro-vascular research such as cardiovascular disease (CVD), coronary heart disease (CHD) and stroke, using pattern analysis and segmentation analysis.
- 2018: Complications due to micro-vascular research such as chronic kidney disease (CKD), bladder, foot, and eye issues such as diabetic retinopathy (DR).
- 2019: CGM big data analysis, using wave theory, energy theory, frequency domain analysis, quantum mechanics, and AI.
- 2020: Cancer, dementia, longevity, geriatrics, DR, hypothyroidism, diabetic foot, diabetic fungal infection, linkage between metabolism and immunity, and learning about certain infectious diseases such as COVID-19.
- 2021: Applications of linear elastic glucose theory (LEGT) and perturbation theory from quantum mechanics on medical research subjects, such as chronic diseases and their complications, cancer, and dementia. Using metabolism and immunity.it's as the base, he expands his research into cancers, semantic, and COVID-19.

To date, he has collected more than two million data regarding his medical conditions and lifestyle details. In addition, he has written 498 medical papers and published 400+ articles in 100+ various medical journals, including 6 special editions with selected 20-25 papers for each edition. Moreover, he has given ~120 presentations at ~65 international medical conferences. He has continuously dedicated time and effort on medical research work and shared his findings and learnings with other patients worldwide.

## Metabolism Index Model Using GH-Method: Math-Physical Medicine

Topology is a newer branch of mathematics which was created around 1900. It studies key properties of "spaces", such as metabolism of the human body space, which are invariant under any continuous deformation happened during the lifespan. A few key properties or characteristics are not going to change as long as the space itself is not encountering a "breaking" situation, such as operational discontinuity of organs or death (death is a total "broken" case). Topology optimization is a mathematical method that optimizes material layout within a given design space, for a given set of loads/forces, boundary conditions and constraints with the goal of maximizing the performance of the system. As a matter of fact, topology optimization has been applied by engineers to obtain the best layout design and expected performance of some automotive components. When we look at human organs and try to determine how to achieve certain predetermined health goals, we recognize that the human metabolism is also a related form of the "topology optimization". This problem can be solved by using available mathematical programming methods in combination with finite element engineering modeling method from structural and mechanical engineering disciplines. They can be used in conducting the targeted analysis in order to obtain an optimized human organ performance or human organ's biochemical response.

Based on the above learned academic knowledge and acquired professional experience, the author spent the entire year of 2014 to develop a mathematical metabolism model. This human metabolism model consists of a total of 10 categories, including 4-categories of disease conditions (body outputs, like deformation/strain) and 6-categories of lifestyle details (body inputs, like force/stress). Similar to an engineering finite element model, these 10 categories further consist of around 500 detailed elements. Finally, by utilizing complicated mathematical derivations and multiple programming techniques, he was able to proceed the topological response analysis and obtain his developed 14-page output sheets which was then used in 2014 for the software programming work. This application software development task is a rather sophisticated job that provides an approximated estimation of human metabolism situation.

A physical analogy of this mathematical metabolism model is similar to "using a finite number of nails that are encircled by millions rubber bands". For example, at first, we hammer 10 nails into a piece of flat wood with an initial shape of a circle with a center in the middle of the circle, then take 3,628,800 (=10!) rubber bands to encircle all of these 10 nails, starting with 2 nails, and then 2+ nails, and finally enclosing all of these 10 nails. These ~3.6 million rubber bands represent the maximum possible relationships existing among these 10 nails. In other words, a small number of data elements of 10 would create a huge number of possible relationships to connect these 10 data elements. Some rubber bands encircle 2 nails, or 3 nails, and so on, until the last rubber band encircles all of the 10 nails together (no rubber band to encircle a single nail is allowed). Now, if we move any one of the nails outward (i.e., moving away from the center of the nail circle), then this moving action would create some internal tension (or stretch force) inside the encircled rubber band. Moving one particular nail "outward" means one of these ten metabolism categories is becoming "unhealthy" which would cause some internal stress to our body. Of course, we can also move some or all of these 10 nails outward at the same time, and with different moving scale for each nail. If we can measure and calculate the summation of all of these internal tensions which are created inside of the affected rubber bands, then this summarized tension force is equivalent to the total metabolism value of human health. The higher tension means the higher metabolism value which creates an unhealthy situation. The author uses the above-described physical scenario of moving nails and estimating tensions inside the encircled rubber bands to explain his developed model of mathematical metabolism for human health.

At first, he developed a medical software APP on his iPhone in 2011, he then began collecting his own health data of weight and glucose since 1/1/2012. After that, he started category by category to enter his other medical conditions, e.g., blood pressure, lipid, etc. and detailed lifestyle data for the period of 2013 to 2014. By now 8/7/2021, he has already collected more than 2 million data regarding his own body health and lifestyle details. Finally, by the end of 2014, he compiled all of his available big data together and expressed them in terms of two newly defined biomedical terms: the metabolism index (MI), which is a combined daily score to show the body health situation, and general health status unit (GHSU), which is the 90-days moving average number to show the health trend. He has also identified a "break-even line or point" at 0.735 or 73.5% to separate his metabolic conditions between the healthy state (below 0.735) and unhealthy state (above 0.735). This set of "Break-even conditions" applies on his original MI model only.

## The Consensus Report of T2D Remission

From 2009 to 2021, the ADA convened an international, multidisciplinary expert group. Representatives from the ADA, European Association for the Study of Diabetes, Diabetes UK, the Endocrine Society, and the Diabetes Surgery Summit, with one additional oncologist were included.

The following is a long excerpt from the "Consensus Report: Definition and Interpretation of Remission in Type 2 Diabetes" by Matthew C Riddle, William T Cefalu, Philip H Evans, Hertzel C Gerstein, Michael A Nauck, William K Oh, Amy E Rothberg, Carel W le Roux, Francesco Rubino, and other authors, published on August 30, 2021, in the The Journal of Clinical Endocrinology & Metabolism. The original paper has 6,328 words. The author considers this paper as a trove of knowledge; therefore, he has kept ~40% of its original words (2,500 words) in this excerpt for future access.

## Abstract

This group proposed "remission" as the most appropriate descriptive term, and HbA1C < 6.5% (48 mole/mol) measured at least 3 months after cessation of glucose-lowering pharmacotherapy as the usual diagnostic criterion.

## Consensus Statement

The natural history of type 2 diabetes (T2D) is clearly heterogeneous, with both genetic and environmental factors contributing to its pathogenesis and evolution. Typically, a genetic predisposition is present at birth but the hyperglycemia that defines diabetes appears only gradually and reaches diagnostic levels in adulthood. Environmental factors modulating expression of T2D include availability of various foods; opportunity for and participation in physical activity; stress related to family, work, or other influences; exposure to pollutants and toxins; and access to public health and medical resources.

T2D that has developed gradually and independent of these stimuli, but most often accompanying weight gain in midlife, can become easier to control or appear to remit following weight loss in some cases.

Significant behavioral changes mainly related to nutrition and weight management can lead to a return from overt hyperglycemia to nearly normal glucose levels for extended periods of time.

In 2009 a consensus statement initiated by the American Diabetes Association (ADA) addressed these issues. It suggested that "remission," signifying "abatement or disappearance of the signs and symptoms," be adopted as a descriptive term.

## Three categories of remission were proposed.

(1) "Partial" remission was considered to occur when hyperglycemia below diagnostic thresholds for diabetes was maintained without active pharmacotherapy for at least 1 year. (2) "Complete" remission was described as normal glucose levels without pharmacotherapy for 1 year. (3) "Prolonged" remission could be described when a complete remission persisted for 5 years or more without pharmacotherapy.

A level of HbA1c <6.5% (<48 mmol/mol) and/or fasting plasma glucose (FPG) 100–125 mg/dL (5.6 to 6.9 mmol/L) were used to define a partial remission, while "normal" levels of HbA1c and FPG (<100 mg/dL [5.6 mmol/L]) were required for a complete remission.

To build upon this statement and subsequent publications in the context of more recent experience, the ADA convened an international, multidisciplinary expert group. Representatives from the American Diabetes Association, European Association for the Study of Diabetes, Diabetes UK, the Endocrine Society, and the Diabetes Surgery Summit were included. For another perspective, an oncologist was also part of the expert group. This group met three times in person and conducted additional electronic exchanges between February 2019 and September 2020. The following is a summary of these discussions and conclusions derived from them.

## Optimal Terminology

In T2D, the terms resolution, reversal, remission, and cure each have been used to describe a favorable outcome of interventions resulting in a disease-free status. In agreement with the prior consensus group's conclusions, this expert panel concluded that diabetes remission is the most appropriate term. Remission is a term widely used in the field of oncology (18), defined as a decrease in or disappearance of signs and symptoms of cancer. Diabetes is defined by hyperglycemia, which exists on a continuum. One reason for this decision was that the underlying pathophysiology of T2D, including both deficiency of insulin and resistance to insulin's actions, as well as other abnormalities, is rarely completely normalized by interventions. In addition, any criterion for identifying a remission of diabetes will necessarily be arbitrary, a point on a continuum of glycemic levels. A single definition of remission based on glycemic measurements was thought more likely to be helpful. The term reversal is used to describe the process of returning to glucose levels below those diagnostic of diabetes, but it should not be equated with the state of remission.

### Glycemic Criteria for Diagnosing Remission of T2D

Measures widely used for diagnosis or glycemic management of T2D include HbA1c, FPG, 2-h plasma glucose after an oral glucose challenge, and mean daily glucose as measured by continuous glucose monitoring (CGM). The group favored HbA1c below the level currently used for initial diagnosis of diabetes, 6.5% (48 mmol/mol), and remaining at that level for at least 3 months without continuation of the usual antihyperglycemic agents as the main defining measurement. However, a number of factors can affect HbA1c measurements, including a variant hemoglobin, differing rates of glycation, or alterations of erythrocyte survival that can occur in a variety of disease states. Information on which methods are affected by variant hemoglobins can be found at http://ngsp.org/interf.asp. Thus, in some people a normal HbA1c value may be present when glucose is actually elevated, or HbA1c may be high when mean glucose is normal. In settings where HbA1c may be unreliable, measurement of 24-h mean glucose concentrations by CGM has been proposed as an alternative. A glycated hemoglobin value calculated as equivalent to the observed mean glucose by CGM has been termed the estimated HbA1c (eA1C) (25) or most recently a glucose management indicator (GMI) (26). In cases where the accuracy of HbA1c values is uncertain, CGM can be used to assess the correlation between mean glucose and HbA1c and identify patterns outside the usual range of normal (27, 28).

Considering all alternatives, the group strongly favored use of HbA1c $< 6.5\%$ (48 mmol/mol) as generally reliable and the simplest and most widely understood defining criterion under usual circumstances. In some circumstances, an eA1C or GMI $< 6.5\%$ can be considered an equivalent criterion.

### Can Remission Be Diagnosed While Glucose-Lowering Drugs Are Being Used?

Diabetes remission may be achieved by a change of lifestyle, other medical or surgical interventions, or, as is often the case, a combination of these approaches.

Alterations of lifestyle involving day-to-day routines related to nutrition and physical activity have health effects that extend well beyond those related to diabetes. Moreover, the possibility of not only achieving diabetes remission but also generally improving health status may have motivated the individual to make these changes in the first place.

Whether a remission can be diagnosed in the setting of ongoing pharmacotherapy is a more complex question. If antihyperglycemic drug therapy continues, it is not possible to discern whether a drug-independent remission has occurred. A diagnosis of remission can only be made after all glucose-lowering agents have been withheld for an interval that is sufficient both to allow waning of the drug's effects and to assess the effect of the absence of drugs on HbA1c values.

This is a controversial area, with arguments both for and against. In favor of pharmacotherapy to prevent emergence or re-emergence of overt diabetes is the possibility of safely and inexpensively eliminating a period of undiagnosed yet harmful hyperglycemia (30). On the other side is the argument that protection against β-cell deterioration by pharmacotherapy has yet to be convincingly proven and preventive intervention has known costs and potential risks.

### Temporal Aspects of Diagnosing Remission

When intervention in T2D is by pharmacotherapy or surgery, the time of initiation is easily determined and the clinical effects are rapidly apparent (Table 1). When intervention is by alteration of lifestyle, the onset of benefit can be slower, and up to 6 months may be required for stabilization of the effect. A further temporal factor is the approximately 3 months needed for an effective intervention to be entirely reflected by the change of HbA1c, which reflects mean glucose over a period of several months. Considering these factors, an interval of at least 6 months after initiation of a lifestyle intervention is needed before testing of HbA1c can reliably evaluate the response. After a more rapidly effective surgical intervention, an interval of at least 3 months is required while the HbA1c value stabilizes. When the intervention is with temporary pharmacotherapy, or when a lifestyle or metabolic surgery intervention is added to prior pharmacotherapy, an interval of at least 3 months after cessation of any glucose-lowering agent is required. With all interventions leading to remission, subsequent measurements of HbA1c not more often than every 3 months nor less frequent than yearly are advised to confirm continuation of the remission. In contrast to HbA1c, FPG or eA1C derived from CGM can stabilize at a shorter time after initiation of an intervention, or increase more rapidly if glycemic control worsens later on. When these measurements of glucose are substituted for HbA1c, they can be collected sooner after the intervention and more frequently thereafter, but because they are more variable, a value consistent with onset or loss of a remission should be confirmed by a repeated measurement.

**Table 1: Interventions and Temporal Factors in Determining Remission of T2D**

| Intervention | Interval before testing of HbA1c can reliably evaluate the response | Subsequent measurements of HbA1c to document continuation of a remission |
|---|---|---|
| Note: Documentation of remission should include a measurement of HbA1c just prior to intervention | | |
| Pharmacotherapy | At least 3 months after cessation of this intervention | Not more often than every 3 months nor less frequent than yearly |
| Surgery | At least 3 months after the procedure and 3 months after cessation of any pharmacotherapy | |
| Lifestyle | At least 6 months after beginning this intervention and 3 months after cessation of any pharmacotherapy | |

Physiologic Considerations Regarding Remissions Following Intervention with Pharmacotherapy, Lifestyle, or Metabolic Surgery When a remission is documented after temporary use of glucose-lowering agents, the direct effects of pharmacotherapy do not persist. Reversal of the adverse effects of poor metabolic control (32) on insulin secretion and action may establish a remission, but other underlying abnormalities persist and the duration of the remission is quite variable. In contrast, when a persistent change of lifestyle leads to remission, the change in food intake, physical activity, and management of stress and environmental factors can favorably alter insulin secretion and action for long periods of time. In this setting, long-term remissions are possible, but not assured. Partial regain of weight can occur, and continuing decline of β-cell capacity may contribute to rising levels of glucose over time.

### Ongoing Monitoring

A remission is a state in which diabetes is not present but which nonetheless requires continued observation because hyperglycemia frequently recurs. Weight gain, stress from other forms of illness, and continuing decline of β-cell function can all lead to recurrence of T2D. Testing of HbA1c or another measure of glycemic control should be performed no less often than yearly. Ongoing attention to maintenance of a healthful lifestyle is needed. The metabolic memory, or legacy effect, is relevant in this setting. These terms describe the persisting harmful effects of prior hyperglycemia in various tissues. Even after a remission, the classic complications of diabetes—including retinopathy, nephropathy, neuropathy, and enhanced risk of cardiovascular disease—can still occur. Hence, people in remission from diabetes should be advised to have regular retinal screening, tests of renal function, foot evaluation, and measurement of blood pressure and weight in addition to ongoing monitoring of HbA1c. At present, there is no long-term evidence indicating that any of the usually recommended assessments for complications can safely be discontinued. Individuals who are in remission should be advised to remain under active medical observation including regular check-ups.

In addition to continued gradual progression of established complications of T2D, there is another risk potentially associated with a remission. This is the possibility of an abrupt worsening of microvascular disease following a rapid reduction of glucose levels after a long period of hyperglycemia. In particular, when poor glycemic control is present together with retinopathy beyond the presence of microaneurysms, rapid reduction of glucose levels should be avoided and retinal screening repeated if a rapid decline in blood glucose is observed.

### Further Questions and Unmet Needs

Validation of Using 6.5% HbA1c as the Defining Measurement The relative effectiveness of using 6.5% HbA1c (48 mmol/mol) as the cut point for diagnosis of remission, as opposed to 6.0% HbA1c (42 mmol/mol), HbA1c 5.7% (39 mmol/mol), or some other level, in predicting risk of relapse or of microvascular or cardiovascular complications should be evaluated. The use of CGM-derived data to adjust HbA1c target ranges for identifying glycemic remission should be further explored. Use of CGM-derived average glucose judged equivalent to HbA1c <6.5% (<48 mmol/mol) or use of FPG < 7.0 mmol/L (<126 mg/dL) instead of HbA1c could be studied.

### Validation of the Timing of Glycemic Measurements

Less frequent testing of HbA1c might be possible without altering predictive efficiency. For example, routine measurements at 6 months and 12 months might be sufficient to identify remission and risk of relapse in the short term.

### Evaluation of Nonglycemic Measures During Remission

Improved glycemic control is not the only aspect of metabolism that may affect long-term outcomes. For example, circulating lipoprotein profiles, peripheral and visceral adiposity, and intracellular fat deposition in the liver and other tissues may all be relevant effects accompanying or possibly separate from glycemic remission and could be evaluated.

### Research on Duration of Remission

The expected duration of a remission induced by various interventions is still not well defined, and factors associated with relapse from remission should be examined more fully.

### Documentation of Long-Term Outcomes After Remission

Long-term effects of remission on mortality, cardiovascular events, functional capacity, and quality of life are unknown. Metabolic and clinical factors related to these outcomes during remission are poorly understood and could be defined.

## Conclusions

A return to normal or nearly normal glucose levels in patients with typical T2D can sometimes be attained by using current and emerging forms of medical or lifestyle interventions or metabolic surgery. The frequency of sustained metabolic improvement in this setting, its likely duration, and its effect on subsequent medical outcomes remain unclear. To facilitate clinical decisions, data collection, and research regarding outcomes, more clear terminology describing such improvement is needed. On the basis of our discussions, we propose the following:

1. The term used to describe a sustained metabolic improvement in T2D to nearly normal levels should be remission of diabetes.
2. Remission should be defined as a return of HbA1c to < 6.5% (<48 mmol/mol) that occurs spontaneously or following an intervention and that persists for at least 3 months in the absence of usual glucose-lowering pharmacotherapy.
3. When HbA1c is determined to be an unreliable marker of chronic glycemic control, FPG < 126 mg/dL (<7.0 mmol/L) or eA1C < 6.5% calculated from CGM values can be used as alternate criteria.
4. Testing of HbA1c to document a remission should be performed just prior to an intervention and no sooner than 3 months after initiation of the intervention and withdrawal of any glucose-lowering pharmacotherapy.
5. Subsequent testing to determine long-term maintenance of a remission should be done at least yearly thereafter, together with the testing routinely recommended for potential complications of diabetes.
6. Research based on the terminology and definitions outlined in the present statement is needed to determine the frequency, duration, and effects on short- and long-term medical outcomes of remissions of T2D using available interventions.

This Consensus Report is jointly published in The Journal of Clinical Endocrinology & Metabolism, published by Oxford University Press on behalf of the Endocrine Society; Diabetologia, published by Springer-Verlag, GmbH, on behalf of the European Association for the Study of Diabetes; Diabetic Medicine, published by Wiley on behalf of Diabetes UK; and Diabe-

tes Care, published by the American Diabetes Association.



### *The Author'S Learned Key-Points from the Consensus Report*

After reading the report five times and absorbing its excellent content, the author attempts to re-write certain selected phrases into the conclusions of this paper. He has summarized the ADA 2021 consensus points, while excluding some of the ADA 2019 consensus points, such as the prolonged remission, etc. *His only intervention is through a stringent and persistent 7 to 10-year long lifestyle management program, without any medications or surgeries.*

Listed below are six conclusions regarding the "remission" of his T2D:

1. The sustained metabolic improvement in T2D to nearly normal levels, HbA1C < 6.5%, FPG < 126 mg/dL, and eA1C < 6.5% should be considered as "remission" of diabetes.
2. A return of HbA1c to < 6.5% that occurs following a lifestyle improvement intervention which persists for at least 3 months in the absence of usual diabetes medications.
3. In addition to HbA1c (when it is determined to be an unreliable or questionable biomarker of chronic glycemic control), FPG < 126 mg/dL or eA1C < 6.5% calculated from CGM values are also used as alternate or additional criteria.
4. Testing of HbA1c should be performed just prior to an intervention and no sooner than six months after withdrawal of any glucose pharmacotherapy.
5. Subsequent testing to determine long-term maintenance of a remission are done near quarterly thereafter, together with other necessary tests routinely for other potential complications of diabetes, such as CVD, CKD, DR, neuropathy, hypothyroidism, etc.
6. This research work based on the terminology and definitions outlined in the present statement is needed to determine the frequency, duration, and effects on short-term and long-term medical outcomes of remissions of T2D. However, in the author's case, he uses the lifestyle intervention exclusively and does not adopt any medical intervention related to medication or surgery.

The following data analyses and their results are based on these six conclusions.

## Results

The four different timespans of Figure 1 show the history of the author's mean finger daily glucose (eAG) since 1/1/2020. His eAG was at 278 mg/dL in 2010, 126 mg/dL in 2012, 121 mg/dL in 2015, and is at 104 mg/dL in 2021. It should be pointed out that his CGM eAG in 2021 is at 113 mg/dL which is ~9% higher than his finger eAG in 2021. This figure indicates that ***his eAG has been continuously improved throughout these past 12 years.***

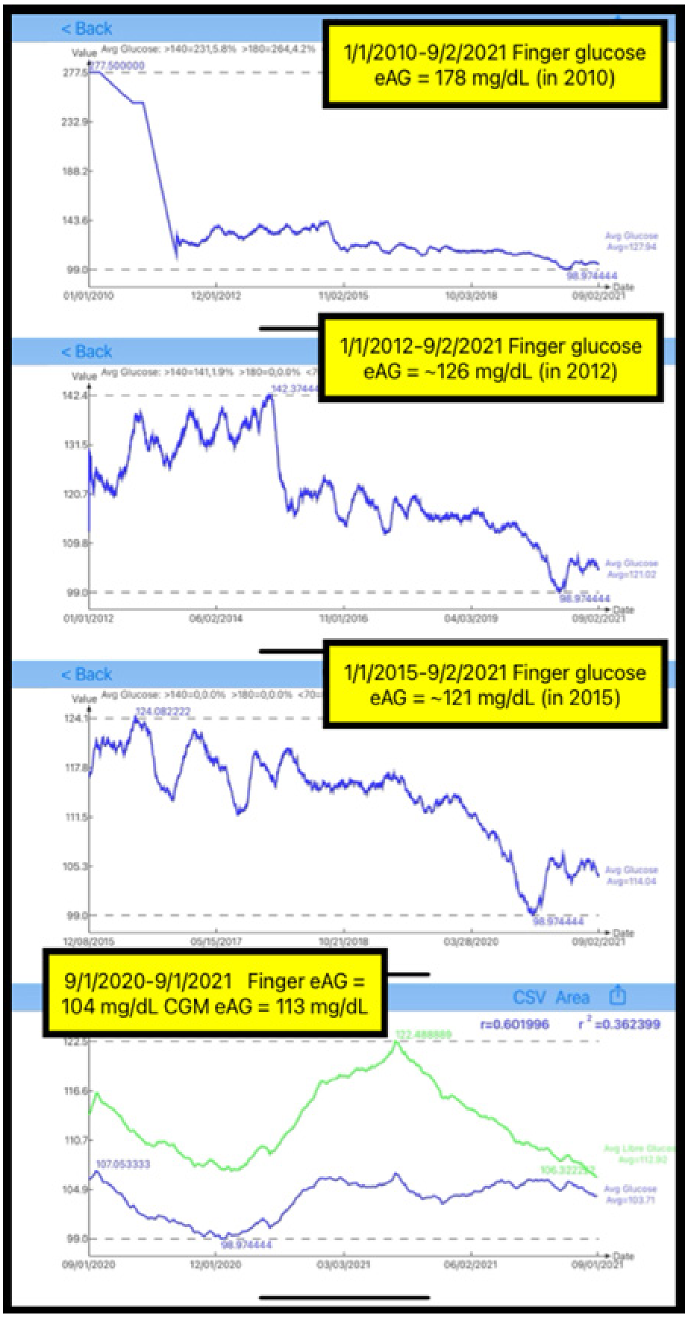



**Figure 1:** Finger eAG for 4 different periods

Figure 2 depicts his FPG and diet/exercise *during the selected year* from 9/1/2020 to 9/1/2021. The following data table lists his average values during this period:

***Carbs/sugar intake = 13.7grams***
***Post-meal walking = 4466 steps***
***CGM PPG = 117 mg/dL***
***CGM FPG = 101 mg/dL***

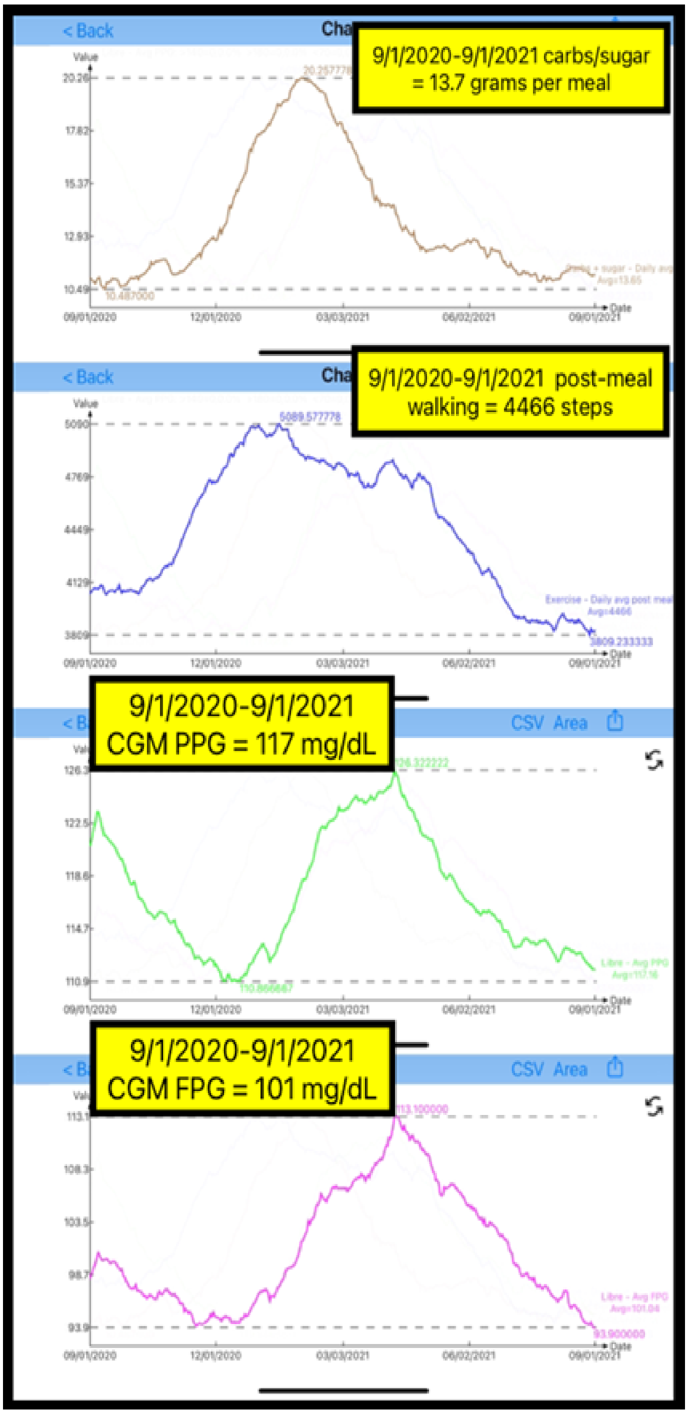
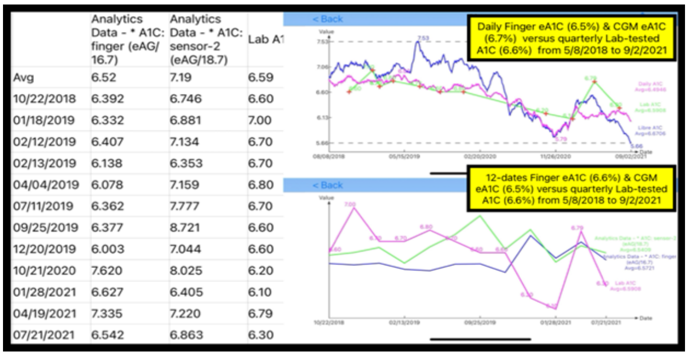



**Figure 2: Carbs/sugar, post-meal walking, CGM PPG, and CGM FPG for 9/1/20-9/1/21**

**The combination of carbs/sugar and walking steps determines his CGM PPG value *while the CGM FPG value of 101 mg/dL (< 126 mg/dL) reflects the pancreatic beta cells health state.***

**Figure 3 illustrates his two estimated HbA1C based on the mean finger glucoses and mean CGM glucoses, i.e., Finger eA1C and CGM eA1C. He uses the following two simple arithmetic formulas to calculate the eA1C values:**

*Finger eA1C = Finger eAG / 16.7*
*CGM eA1C = CGM eAG / 18.7*



| | Analytics Data - * A1C: finger (eAG/ 16.7) | Analytics Data - * A1C: sensor-2 (eAG/18.7) | Lab A1 |
|---|---|---|---|
| Avg | 6.52 | 7.19 | 6.59 |
| 10/22/2018 | 6.392 | 6.746 | 6.60 |
| 01/18/2019 | 6.332 | 6.881 | 7.00 |
| 02/12/2019 | 6.407 | 7.134 | 6.70 |
| 02/13/2019 | 6.138 | 6.353 | 6.70 |
| 04/04/2019 | 6.078 | 7.159 | 6.80 |
| 07/11/2019 | 6.362 | 7.777 | 6.70 |
| 09/25/2019 | 6.377 | 8.721 | 6.60 |
| 12/20/2019 | 6.003 | 7.044 | 6.60 |
| 10/21/2020 | 7.620 | 8.025 | 6.20 |
| 01/28/2021 | 6.627 | 6.405 | 6.10 |
| 04/19/2021 | 7.335 | 7.220 | 6.79 |
| 07/21/2021 | 6.542 | 6.863 | 6.30 |



**Figure 3:** HbA1C comparison for 3.4-year period (8/8/18-9/1/21)

The top diagram reveals the comparison of his 2 eA1C values using daily calculated data against his lab-tested H1C values ***over a longer period of 3.4 years from 5/5/2018 to 9/12/2021.***

***Finger eA1C = 6.5%***
***CGM eA1C = 6.7%***
***Lab eA1C = 6.6%***

The bottom diagram shows the comparison of his 2 eA1C values against his lab-tested H1C values ***on the 12 lab-tested dates over the same longer period of 3.4 years from 5/5/2018 to 9/12/2021.***

***Finger eA1C = 6.6%***
***CGM eA1C = 6.5%***
***Lab eA1C = 6.6%***

Figure 4 exhibits the ***conclusive diagram*** of this study *to determine, at present time, whether his T2D situation belongs to a "remission" state or not. The selected timespan of all judgmental data is from the past one year from 9/1/2010 to 9/1/2021.* He uses three criteria to make his final judgement of "remission", i.e., HbA1C, FPG, and eA1C.

The following table lists his results:

***Lab-tested HbA1C = 6.3% (<6.5%)***
***Finger FPG = 94 mg/dL (<126)***
***CGM FPG = 101 mg/dL (<126)***
***Finger eA1C = 6.2% (<6.5%)***
***CGM eA1C = 6.0% (<6.5%)***

***Based on the above findings, his present T2D situations indeed belongs to a "remission" state***

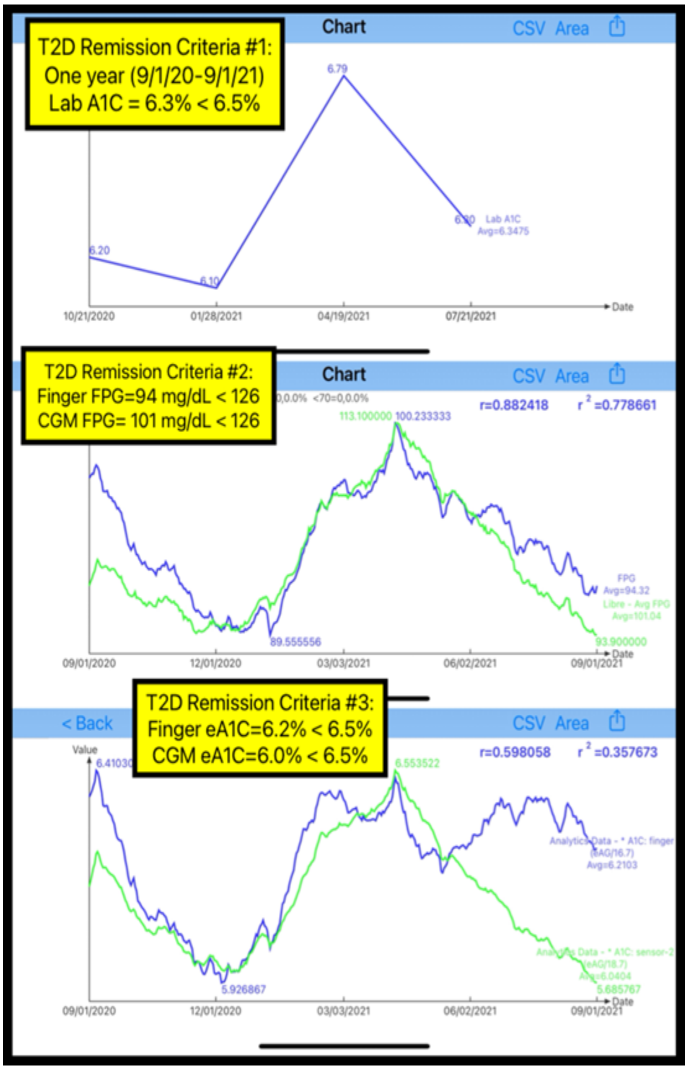



**Figure 4:** Remission examination using HbA1C, FPG, and eA1C for the period of 9/1/2020-9/1/2021

## Conclusion

In conclusion, according to the American Diabetes Association (ADA) 2021 consensus report, the author is in a "remission" state of T2D. In summary, over the selected one-year period from 9/1/2020 to 9/1/2021, his average Lab-A1C is 6.3%, FPG values are 94 mg/dL (finger FPG) and 101 mg/dL (CGM FPG), and CGM eAG is 6.0%.

First, his selected timespan of past one year satisfies the timespan requirement from 2021 consensus report. This set of his glucose data is almost 5 years post-cessation of his medication intervention and initiation of his stringent lifestyle management program.

Second, all of his A1C values are less than 6.5% and his FPG levels are less than 126 mg/dL.

Finally, he has kept his regular routines of having quarterly medical examinations to watch out for various diabetes complications, including macro-vascular, micro- vascular, neural, and hormone systems.

He understands and agree with the consensus report that diabetes is non-curable and at most it is "controllable" or "partially reversible". Nevertheless, as a personal decision made in 2010, he has adopted a lifestyle improvement approach of dealing with the root causes of metabolic disorders, instead of suppressing the external symptoms of diseases through different medical treatments, including both medication and surgery.

## References

For editing purposes, majority of the references in this paper, which are self-references, have been removed for this article. Only references from other authors' published sources remain. The bibliography of the author's original self-references can be viewed at www.eclairemd.com.

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